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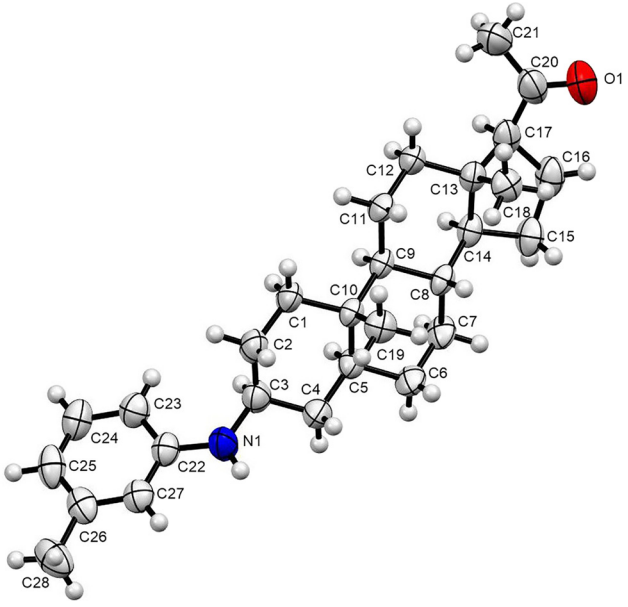
Synthesis and crystal structure of 1-((3*R*,10*S*,13*S*,17*S*)-10,13-dimethyl-3-(*m*-tolylamino) hexadecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)ethan-1-one, $C_{28}H_{41}NO$



https://doi.org/10.1515/ncrs-2023-0105
Received March 7, 2023; accepted March 24, 2023;
published online April 13, 2023

Abstract

$C_{28}H_{41}NO$, triclinic, *P*1 (no. 1), a = 6.3144(8) Å, b = 9.7315(13) Å, c = 10.5867(14) Å, α = 111.561(4)°, β = 96.486 (4)°, γ = 97.128(4)°, V = 591.41(14) Å^3, Z = 1, $R_{gt}(F)$ = 0.0579, $wR_{ref}(F^2)$ = 0.1687, T = 273(2) K.

CCDC no.: 2246864

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.23 × 0.20 × 0.18 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.07 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	35.6°, 98%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	29,665, 10,643, 0.050
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 4969
$N(param)_{refined}$:	275
Programs:	Olex2 [1], Bruker [2], SHELX [3], Diamond [4]

1 Source of material

In methanol (10 mL) with 5α-pregnane-3,20-dione (1.6 mmol) and *m*-methylaniline (1.3 mmol) and 1 drop of acetic acid, the reaction was stirred for 24 h at room temperature. Then sodium borohydride (3.9 mmol) was added to stir for 3 h and the solid product was obtained by reduced pressure. Using ethyl acetate for extraction, add dilute sodium hydroxide to adjust the organic solvent as weak alkaline, then combined organic layer was dried over anhydrous Na_2SO_4, the crude product was obtained by evaporation under reduced pressure, and then the colorless and transparent crystals were obtained by recrystallization using methanol. 47% yield. Elemental analysis calcd. (%) for $C_{28}H_{41}NO$: C, 82.50; H, 10.14; N, 3.44; O, 3.92.

2 Comment

The pregnant steroid alkaloid is the main active component of the *Sarcococca ruscifolia* and its *Sarcococca hookeriana*, this type of compound has antibacterial, antitumor and significant anticholinesterase inhibition [5–7]. A series of progesterone alkaloids were isolated from *S. ruscifolia* with inhibitory activity on tumor cells [8–10]. In order to find high-efficient and low-toxic pregnane steroidal alkaloid

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.3977 (3)	0.3899 (3)	0.4830 (2)	0.0580 (5)
C2	0.4134 (4)	0.2901 (3)	0.3364 (3)	0.0660 (6)
C3	0.5357 (4)	0.3772 (3)	0.2645 (2)	0.0626 (6)
C4	0.7569 (4)	0.4556 (3)	0.3507 (2)	0.0636 (6)
C5	0.7349 (3)	0.5587 (2)	0.4958 (2)	0.0532 (5)
C6	0.9502 (4)	0.6565(3)	0.5788 (2)	0.0655 (6)
C7	0.9194 (4)	0.7696 (3)	0.7155 (3)	0.0623 (6)
C8	0.8023 (3)	0.6947 (2)	0.7991 (2)	0.0482 (4)
C9	0.5854 (3)	0.5940 (2)	0.7120 (2)	0.0455 (4)
C10	0.6183 (3)	0.4744 (2)	0.5742 (2)	0.0452 (4)
C11	0.4537 (3)	0.5303 (3)	0.7978 (2)	0.0574 (5)
C12	0.4256 (3)	0.6487 (3)	0.9350 (2)	0.0586 (5)
C13	0.6450 (3)	0.7380 (2)	1.0210 (2)	0.0506 (5)
C14	0.7597 (3)	0.8082 (2)	0.9327 (2)	0.0510 (5)
C15	0.9502 (4)	0.9224 (3)	1.0348 (3)	0.0683 (6)
C16	0.8640 (5)	0.9831 (3)	1.1697 (3)	0.0742 (8)
C17	0.6437 (4)	0.8823 (3)	1.1511 (2)	0.0630 (6)
C18	0.7770 (4)	0.6357 (3)	1.0651 (3)	0.0619 (5)
C19	0.7492 (4)	0.3612 (3)	0.6009 (3)	0.0597 (5)
C20	0.6025 (5)	0.8535 (4)	1.2784 (3)	0.0785 (8)
C21	0.3787 (5)	0.7898 (5)	1.2826 (3)	0.0927 (10)
C22	0.3938 (4)	0.2477 (3)	0.0107 (2)	0.0582 (5)
C23	0.2002 (4)	0.3021 (3)	0.0190 (3)	0.0659 (6)
C24	0.0503 (5)	0.2646 (3)	−0.1018 (3)	0.0733 (7)
C25	0.0917 (5)	0.1728 (3)	−0.2267 (3)	0.0751 (8)
C26	0.2823 (4)	0.1180 (3)	−0.2354 (2)	0.0662 (6)
C27	0.4297 (4)	0.1554 (3)	−0.1170 (3)	0.0619 (5)
C28	0.3295 (7)	0.0177 (4)	−0.3736 (3)	0.0950 (10)
H2	0.286160	0.861779	1.285845	0.139*
H2A	0.268610	0.245986	0.284028	0.079*
H3	−0.009967	0.147496	−0.306053	0.090*
H4	−0.078205	0.302238	−0.097239	0.088*
H5	0.557943	0.117436	−0.122952	0.074*
H6	0.466386	0.059277	−0.387947	0.143*
H7	0.217260	0.011219	−0.445791	0.143*
H10	0.454228	0.455106	0.259918	0.075*
H11	1.048614	0.593444	0.594993	0.079*
H12	0.836240	0.840490	0.698906	0.075*
H13	1.059874	0.825148	0.768663	0.075*
H14	0.994145	1.002413	1.004148	0.082*
H15	1.073146	0.874494	1.045246	0.082*
H16	0.845375	1.086204	1.191010	0.089*
H17	0.964709	0.980306	1.244709	0.089*
H18	0.692383	0.585540	1.110549	0.093*
H19	0.907108	0.695209	1.127129	0.093*
H20	0.814098	0.562491	0.985159	0.093*
H23	0.307670	0.462744	0.479629	0.070*
H24	0.487086	0.208983	0.338372	0.079*
H26	0.326338	0.328399	0.525568	0.070*
H27	0.670504	0.308897	0.647208	0.090*
H28A	0.886728	0.413822	0.657458	0.090*
H28	0.334774	−0.080802	−0.374485	0.143*
H29	0.771896	0.290263	0.514628	0.090*
H30	0.500138	0.660506	0.686808	0.055*
H31	0.337780	0.716762	0.917205	0.070*
H32	0.350606	0.599686	0.986402	0.070*
H33	0.326434	0.699976	1.201641	0.139*
H34	0.378566	0.766365	1.363154	0.139*
H35	0.528986	0.932510	1.127728	0.076*
H36	0.660551	0.866654	0.906250	0.061*
H37	0.894672	0.630465	0.822186	0.058*
H38	1.014484	0.709055	0.526429	0.079*
H39	0.641409	0.627665	0.483713	0.064*
H40	0.842402	0.381166	0.356432	0.076*
H41	0.831871	0.514158	0.306941	0.076*
H42	0.170539	0.362625	0.103765	0.079*
H111	0.311500	0.480399	0.743701	0.069*
H112	0.524789	0.455315	0.816455	0.069*
N1	0.5544 (4)	0.2855 (3)	0.1254 (2)	0.0758 (6)
H1	0.673167	0.251874	0.112315	0.091*
O1	0.7441 (5)	0.8789 (4)	1.3745 (3)	0.1231 (10)

derivatives, we have prepared several pregnane steroid alkaloids by modifying the C-3 position of a ring to convert pregnane into alkaloid derivatives [11–13]. For purpose of continuing to synthesize more of these compounds, we introduced *m*-methylaniline at the C-3 position to obtain the novel compound 1-((3*R*,10*S*,13*S*,17*S*)-10,13-dimethyl-3-(*m*-tolylamino)hexadecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-ethan-1-one.

The title compound consists of three six-membered rings, a five-membered ring, two methyl groups, and an *m*-methylaniline. All parameters are in the normal structure range, methyl substituents C10 and C13 on atoms are in the β configuration, *m*-methylaniline in a plane with a root mean square value of 1.441(3) Å. The carbonyl group is confirmed by distance *d*(C20–O1) = 1.205(3) Å.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: Key Projects of Guizhou Basic Research Program [grant number Qiankehejichu–ZK (2022) key 046], the Science and Technology Tip-top Talent Foundation of Universities in Guizhou Province [grant number Qianjiaoke–KY (2021) 034].

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

1. Dolomanov O. V., Bourhis L. J., Gildea R. J., Howard J. A. K., Puschmann H. OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* 2009, *42*, 339–341.
2. Bruker. *APEX2*, *SAINT and SADABS*; Bruker AXS Inc.: Madison, Wisconsin, USA, 2012.
3. Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Brandenburg K. *DIAMOND. Visual Crystal Structure Information System. Ver. 4.0*; Crystal Impact: Bonn, Germany, 2015.
5. Kumar A., Sati S. C., Sati M. D., Kumar S., Singh D., Bhatt U., Kaur G. Chemical and potential biological perspectives of genus *Sarcococca* (Buxaceae). *Nat. Prod. J.* 2015, *5*, 28–49.
6. Khan M. T. H. Putative molecular interactions involving naturally occurring steroidal alkaloids from *Sarcococca hookeriana* against acetyl- and butyryl-cholinesterase. *Curr. Bioinf.* 2013, *8*, 416–428.
7. Zhang P., Shao L. P., Shi Z., Zhang Y., Du J., Cheng K. J., Yu P. Z. Pregnane alkaloids from *Sarcococca ruscifolia* and their cytotoxic activity. *Phytochem. Lett.* 2015, *14*, 31–34.
8. Huo S. J., Wu J. C., He X. C., Pan L. T., Du J. Two new cytotoxic steroidal alkaloids from *Sarcococca hookeriana*. *Molecules* 2018, *24*, 11.
9. He K., Zou J., Wang J. X., Du J. Crystal structure of (*Z*)-*N*-(17-(1-(dimethylamino)ethyl)-10,13-dimethyl-4-oxo-4,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta-[α] phenanthren-3-yl)-3-methylbut-2-enimidic acid dichloromethane monosolvate, $C_{29}H_{45}Cl_2N_2O_2$. *Z. Kristallogr. N. Cryst. Struct.* 2013, *228*, 327–328.
10. He K., Wang J. X., Zou J., Wu J. C., Huo S. J., Du J. Three new cytotoxic steroidal alkaloids from *Sarcococca hookeriana*. *Molecules* 2018, *23*, 1181.
11. Zhang W. W., Ye J. H., Zhou J., He K. Synthesis and crystal structure of 1-((3*R*,10*S*,13*R*,17*S*)-10,13-dimethyl-3-(phenylamino)hexadecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)ethan-1-one, $C_{27}H_{39}NO$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 815–817.
12. Huang H., Zhang W. W., Ye J. H., Zhou J., He K. Synthesis and crystal structure of 1-((3*R*,10*S*,13*R*,17*S*)-10,13-dimethyl-3-(*p*-tolylamino)hexadecahydro-1*H*-cyclopenta[α]phenanthren-17-yl) ethan-1-one, $C_{28}H_{41}NO$. *Z. Kristallogr. N. Cryst. Struct.* 2023, *238*, 31–33.
13. Zhang W. W., Ye J. H., Huang H., Zhou J., He K. Synthesis and crystal structure of 1-((3*R*,10*S*,13*R*,17*S*)-3-((4-methoxyphenyl)amino)-10,13-dimethylhexadecahydro-1*H*-cyclopenta [α]-phenanthren-17-yl) ethan-1-one, $C_{28}H_{41}NO_2$. *Z. Kristallogr. N. Cryst. Struct.* 2023, *238*, 189–191.